eurofins | BioPharma Product Testing



Bioburden

Characterization, method validation and determination

Application field

The term bioburden is used to describe the population of viable microorganisms present on or in product and/or a sterile barrier system. Bioburden is the sum of the microbial contributions from a number of sources, including raw materials, manufacturing of components, assembly processes, manufacturing environment, assembly/manufacturing aids (e.g., compressed gases, water, lubricants), cleaning processes and packaging of finished product.

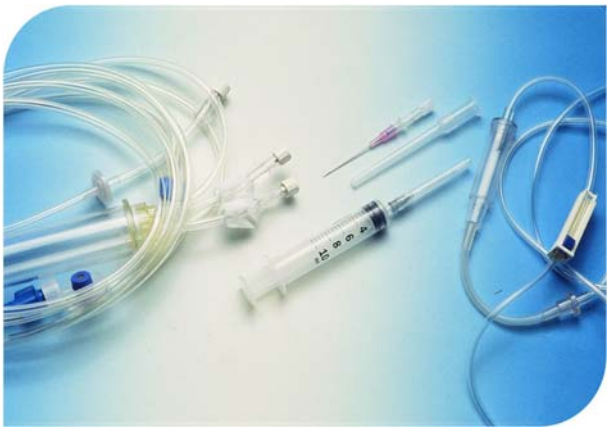
Interests

A knowledge of bioburden can be used in a number of situations as part of:

- Validation and revalidation of sterilization processes;
- Routine monitoring for control of manufacturing processes;
- Monitoring of raw materials, components or packaging;
- Assessment of the efficiency of cleaning processes;
- An overall environmental monitoring program

Principle of the test

Microbial characterization of bioburden (staining properties, cell morphology, colony morphology and so on), a validation of method used to determine the bioburden is performed and a correction factor (numerical value applied to compensate for incomplete removal from product and/or culture of microorganisms) is calculated. Then using the validated method and the calculated correction factor the bioburden is calculated for each device.



Test procedure

The degree of microbial characterization necessary for the bioburden of product is based on the purpose for which the data are used.

The micro-organism are recovered from the device by sonication or stomaching and placed on:

- TSA at 30-35°C for 3 days (for facultative, non-fastidious, aerobic bacteria)
- SDA at 20-25°C for 5 days (for yeasts and moulds)
- TSA at 30-35°C for 3 days in anaerobic condition (for anaerobic bacteria)

Then the characterization is performed verifying:

- colony morphology
- cell morphology
- gram staining

To validate the method there are essentially two approaches available. These approaches are:

- repetitive treatment of a sample product (exhaustive recovery),
- product inoculation with known levels of microorganism,

followed by quantitative assessment of the extent of recovery.

The former needs a relatively high initial bioburden, the latter is indicated when bioburden in low or very low.



For repetitive treatment, the method of bioburden determination (i.e. sonication, stomaching or vortexing) should be repeated until there is no significant increase in the accumulated number of microorganisms recovered. After each repetition, the eluent is totally recovered from the product or product portion and enumerated.
Results accumulated from the consecutive recoveries are compared. It should be noted, however, that this method is not necessarily precise: the exact relationship between the number of microorganisms recovered and the actual number on the product cannot always be demonstrated.

For product inocultaion method, an artificial bioburden can be created by inoculating a known number of a selected microorganism on to product in order to establish recovery efficiency. For example an aqueous suspension of Bacillus atrophaeus is inoculated on the device and allowed to dry under laminar airflow.
The inoculated products were subjected to the chosen removal technique and the mean number of spores removed is determined and the correction factor for recovery efficiency is calculated. Using the validate method and the correction factor, the bioburden is routinely determined.

Normative references

EN ISO 11737-1:2006

Expression of results

Furthermore the EN ISO 11737-1:2006 does not specify requirements for the microbiological monitoring of the environment in which medical devices are manufactured.

Exclusion from test

The reference standard EN ISO 11737-1:2006 does not specify requirements for the enumeration or identification of viral or protozoan contaminants and the requirements specified in this standard are not intended to address the removal and detection of the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeldt-Jakob disease. Furthermore the EN ISO 11737-1:2006 does not specify requirements for the microbiological monitoring of the environment in which medical devices are manufactured.

Turn around time

8 days.

Number of products/Quantity necessary to the analysis

At least, 10 samples for charaterization, 20 for validation and 10 sample/batch for routine determination.